Test Definition: UGTFZ

UDP-Glucuronosyltransferase 1A1 (UGT1A1), Full Gene Sequencing, Varies

Overview

Useful For

Establishing a diagnosis of Crigler-Najjar syndrome type I or type II and the trait of Gilbert syndrome

Establishing carrier status for Crigler-Najjar syndrome type I or type II

Identifying individuals who are at risk of hyperbilirubinemia or who have Gilbert syndrome

Identifying individuals who are at increased risk of adverse drug reactions or hyperbilirubinemia when taking drugs that are metabolized by *UGT1A1*, including atazanavir, belinostat, irinotecan, nilotinib, pazopanib, and sacituzumab govitecan

Identifying individuals who may have increased drug levels when taking dolutegravir or raltegravir

Follow-up testing for individuals with a suspected *UGT1A1* variant, who had negative TA repeat region testing

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This is a full gene sequencing test for *UGT1A1* that includes the TA repeat region of the promoter and all intron/exon boundaries. Results are interpreted for the purposes of UGT1A1 drug metabolism and hereditary hyperbilirubinemia syndromes (Gilbert syndrome and Crigler-Najjar syndrome). This test does not include deletion/duplication analysis of the *UGT1A1* gene.

Testing Algorithm

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

For information see *UGT1A1* Test-Ordering Algorithm.

Special Instructions

- Informed Consent for Genetic Testing
- UGT1A1 Gene Testing Patient Information
- UGT1A1 Test-Ordering Algorithm
- Pharmacogenomic Association Tables
- Informed Consent for Genetic Testing (Spanish)

Highlights

This test screens for *UGT1A1* gene sequence variants associated with increased risk of adverse drug reactions when taking UGT1A1-metabolized drugs. These drugs include atazanavir, belinostat, irinotecan, nilotinib, pazopanib, and sacituzumab govitecan. In addition, sequence variants may impact drug levels for patients taking dolutegravir or raltegravir.

This test screens for *UGT1A1* gene sequence variants associated with congenital hyperbilirubinemia conditions, including Gilbert syndrome, Crigler-Najjar syndrome type I and type II.

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequence Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

If analysis of only the UGT1A1 promoter TA repeat region (*28, *36, *37 alleles) is desired, see U1A1Q / Uridine Diphosphate (UDP) Glucuronosyltransferase 1A1 TA Repeat Genotype, *UGT1A1*, Varies.

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor or a liver transplant will interfere with testing. For information about testing patients who have received a hematopoietic stem cell or liver transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA)
Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated

due to DNA quality will be noted in the report.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. *UGT1A1* Gene Testing Patient Information (T664) is requested but not required.
3. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Therapeutics Test Request (T831)
-Oncology Test Request (T729)

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

The *UGT1A1* gene contains 5 exons and is part of a gene complex located on chromosome 2q37 that encodes several enzymes called uridine diphosphate (UDP)-glucuronosyltransferases. These enzymes perform a chemical reaction called glucuronidation, a major pathway that enhances the elimination of small lipophilic molecules, such as steroids, bilirubin, hormones, and drugs, into water-soluble metabolites that can be excreted from the body.

The UGT1A1 enzyme, primarily found in the liver, is responsible for the glucuronidation of bilirubin, converting it from the toxic form of bilirubin (unconjugated bilirubin) to its nontoxic, water-soluble form (conjugated bilirubin). Genetic variants in *UGT1A1* may cause reduced or absent UGT1A1 enzymatic activity, resulting in conditions associated with unconjugated hyperbilirubinemia, including Gilbert syndrome and Crigler-Najjar syndrome.(1-4)

Gilbert syndrome is the most common hereditary cause of increased bilirubin and is characterized by total serum bilirubin levels of 1 to 6 mg/dL. Gilbert syndrome is generally considered to be an autosomal recessive trait, although autosomal dominant inheritance has been suggested in some cases. Gilbert syndrome is characterized by a 25% to 50% reduction in glucuronidation activity of the UGT1A1 enzyme, along with episodes of mild intermittent jaundice and the absence of liver disease.(1-3)

Crigler-Najjar (CN) syndrome is an autosomal recessive disorder caused by more severe reductions in UGT1A1

glucuronidation activity and can be subdivided into type 1 and type 2 (CN1 and CN2). CN1 is the most severe form, with complete absence of enzyme activity and total serum bilirubin levels of 20 to 40 mg/dL. Infants with CN1 present with jaundice shortly after birth that persists thereafter.(1,2,4) CN2 is milder than CN1, with at least partial UGT1A1 activity and total serum bilirubin ranging from 6 to 20 mg/dL.(1,2,4) Phenobarbital, a drug that induces synthesis of a number of hepatic enzymes, is effective in decreasing serum bilirubin levels by approximately 25% in patients with CN2; CN1 does not respond to phenobarbital treatment. If left untreated, the buildup of bilirubin in a newborn can cause bilirubin-induced brain damage, known as kernicterus. In addition to phenobarbital, treatments of CN may include phototherapy, heme oxygenase inhibitors, oral calcium phosphate and carbonate, and liver transplantation.(1,2,4)

In addition to the role of UGT1A1 in bilirubin metabolism, this enzyme also plays a role in drug metabolism. UGT1A1 is involved in the metabolism of irinotecan, a topoisomerase I inhibitor. Irinotecan is a chemotherapy drug used to treat solid tumors, including colon, rectal, and lung cancers. It is a prodrug that forms an active metabolite, SN-38. SN-38 is normally inactivated by conjugation with glucuronic acid followed by biliary excretion into the gastrointestinal tract. If UGT1A1 activity is impaired or deficient, SN-38 fails to become conjugated with glucuronic acid, increasing the concentration of SN-38. This can result in severe neutropenia and diarrhea, which can be life-threatening.(5-8)

Additional drugs have also been associated with an increased risk for adverse outcomes in patients with reduced UGT1A1 enzyme activity. The US Food and Drug Administration drug labels for belinostat, nilotinib, pazopanib, and sacituzumab govitecan contain warnings for an increased risk (incidence) of adverse outcomes or increased bilirubin in patients who have *UGT1A1* variants associated with reduced activity.(7) The Clinical Pharmacogenetics Implementation Consortium (CPIC) released guidelines for atazanavir treatment, indicating that patients with homozygous *UGT1A1* alleles associated with reduced activity or decreased expression should consider an alternate medication due to a significant risk for developing hyperbilirubinemia (jaundice).(8) Additionally, the concentration of several drugs, including dolutegravir and raltegravir, may be increased in patients with reduced UGT1A1 enzyme activity.(7)

In this assay, the *UGT1A1* promoter, exons, and exon-intron boundaries are assessed for variants.(5)

Reference Values

UGT1A1 Phenotype: TA6/TA6 (Normal). No variants detected.

An interpretive report will be provided.

Interpretation

An interpretive report will be provided that includes assessment of risk for UGT1A1-associated adverse drug reactions as well as interpretation for hyperbilirubinemia syndromes.

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(9) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables. This resource includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Cautions

Clinical Correlations:
If the patient has had an allogeneic hematopoietic stem cell transplant (bone marrow transplant) or a recent non-leukocyte reduced blood transfusion, results may be inaccurate due to the presence of donor DNA. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing. *UGT1A1* genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's *UGT1A1* status. Contact Mayo Clinic Laboratories for information and guidance when testing patients who have received a transplant. Absence of a detectable gene variant does not rule out the possibility that the patient may have a genetic cause for increased unconjugated bilirubin.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:
Rare variants exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Reclassification of Variants:
Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare professionals to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:
Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(9) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools are interpreted with caution and professional clinical judgment.

Clinical Reference

1. Skierka JM, Kotzer KE, Lagerstedt SA, O'Kane DJ, Baudhuin LM. UGT1A1 genetic analysis as a diagnostic aid for individuals with unconjugated hyperbilirubinemia. J Pediatr. 2013;162(6):1146-1152.e11522. doi:10.1016/j.jpeds.2012.11.042

2. Moyer AM, Skierka JM, Kotzer KE, Kluge ML, Black JL, Baudhuin LM. Clinical UGT1A1 genetic analysis in pediatric patients: experience of a reference laboratory. Mol Diagn Ther. 2017;21(3):327-335. doi:10.1007/s40291-017-0265-0
3. Thoguluva Chandrasekar V, Faust TW, John S. Gilbert Syndrome. In: StatPearls [Internet]. StatPearls Publishing; Updated October 5, 2025. Accessed November 14, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK470200/
4. Bhandari J, Thada PK, Yadav D. Crigler Najjar Syndrome. In: StatPearls [Internet]. StatPearls Publishing; Updated February 12, 2024. Accessed November 14, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK562171/
5. Goetz MP, McKean HA, Reid JM, et al. UGT1A1 genotype-guided phase I study of irinotecan, oxaliplatin, and capecitabine. Invest New Drugs. 2013;31(6):1559-1567. doi:10.1007/s10637-013-0034-9
6. Innocenti F, Schilsky RL, Ramirez J, et al. Dose-finding and pharmacokinetic study to optimize the dosing of irinotecan according to the UGT1A1 genotype of patients with cancer. J Clin Oncol. 2014;32(22):2328-2334. doi:10.1200/JCO.2014.55.2307
7. US Food and Drug Administration. Table of Pharmacogenetic Associations. Updated October 26, 2022. Accessed November 14, 2025. Available at www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
8. Gammal RS, Court MH, Haidar CE, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for UGT1A1 and atazanavir prescribing. Clin Pharmacol Ther. 2016;99(4):363-369. doi:10.1002/cpt.269
9. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424

Performance

Method Description

Genomic DNA is extracted from whole blood. The *UGT1A1* gene is amplified by polymerase chain reaction (PCR). The PCR product is then purified and sequenced in both directions using fluorescent dye-terminator chemistry. Sequencing products are separated on an automated sequencer, and the trace files analyzed for sequence variants in the exons and intron/exon boundaries using variant detection software and visual inspection.(Skierka J, O'Kane D. UDP-glucuronosyltransferase 1A1 and the glucuronidation in oncology applications and hyperbilirubinemia. In: Grody WW, Nakamura RM, Kiechle FL, Strom CM, eds. Molecular Diagnostics: Techniques and Applications for the Clinical Laboratory. Academic Press; 2010:409-420)

PDF Report

No

Day(s) Performed

Varies

Report Available

7 to 14 days

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81404

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
UGTFZ	UGT1A1 Full Gene Sequencing, V	93844-9

Result ID	Test Result Name	Result LOINC® Value
618686	Result Summary	50397-9
618687	TA Repeat Result	95143-4
618688	Full Gene Sequence Result	82939-0
618691	Interpretation	69047-9
618692	Method	85069-3
618693	Disclaimer	62364-5
618694	Additional Information	48767-8
618695	Reviewed By	18771-6